

European Heart Journal doi:10.1093/eurheartj/ehu278

ESC/EACTS GUIDELINES





2014 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

Authors/Task Force members: Stephan Windecker* (ESC Chairperson) (Switzerland), Philippe Kolh* (EACTS Chairperson) (Belgium), Fernando Alfonso (Spain), Jean-Philippe Collet (France), Jochen Cremer (Germany), Volkmar Falk (Switzerland), Gerasimos Filippatos (Greece), Christian Hamm (Germany), Stuart J. Head (The Netherlands), Peter Jüni (Switzerland), A. Pieter Kappetein (The Netherlands), Adnan Kastrati (Germany), Juhani Knuuti (Finland), Ulf Landmesser (Switzerland), Günther Laufer (Austria), Franz-Josef Neumann (Germany), Dimitrios J. Richter (Greece), Patrick Schauerte (Germany), Miguel Sousa Uva (Portugal), Giulio G. Stefanini (Switzerland), David Paul Taggart (UK), Lucia Torracca (Italy), Marco Valgimigli (Italy), William Wijns (Belgium), and Adam Witkowski (Poland).

National Cardiac Societies document reviewers: listed in Addenda

The content of these European Society of Cardiology (ESC) Guidelines has been published for personal and educational use only. No commercial use is authorized. No part of the ESC Guidelines may be translated or reproduced in any form without written permission from the ESC. Permission can be obtained upon submission of a written request to Oxford University Press, the publisher of the European Heart Journal and the party authorized to handle such permissions on behalf of the ESC.

Associations: Acute Cardiovascular Care Association (ACCA), European Association for Cardiovascular Prevention & Rehabilitation (EACPR), European Association of Cardiovascular Imaging (EACVI), European Heart Rhythm Association (EHRA), Heart Failure Association of the ESC (HFA).

Working groups: Working Group on Cardiac Cellular Electrophysiology, Working Group on Cardiovascular Magnetic Resonance, Working Group on Cardiovascular Pharmacology and Drug Therapy, Working Group on Cardiovascular Surgery, Working Group on Coronary Pathophysiology and Microcirculation, Working Group on Nuclear Cardiology and Cardiac Computed Tomography, Working Group on Peripheral Circulation, Working Group on Thrombosis, Working Group on Valvular Heart Disease.

Councils: Council for Cardiology Practice, Council on Cardiovascular Primary Care, Council on Cardiovascular Nursing and Allied Professions.

Disclaimer 2014: The ESC Guidelines represent the views of the ESC and were produced after careful consideration of the scientific and medical knowledge and the evidence available at the time of their dating.

The ESC is not responsible in the event of any contradiction, discrepancy and/or ambiguity between the ESC Guidelines and any other official recommendations or guidelines issued by the relevant public health authorities, in particular in relation to good use of healthcare or therapeutic strategies. Health professionals are encouraged to take the ESC Guidelines fully into account when exercising their clinical judgment as well as in the determination and the implementation of preventive, diagnostic or therapeutic medical strategies; however, the ESC Guidelines do not in any way whatsoever override the individual responsibility of health professionals to make appropriate and accurate decisions in consideration of each patient's health condition and, where appropriate and/or necessary, in consultation with that patient and the patient's care provider. Nor do the ESC Guidelines exempt health professionals from giving full and careful consideration to the relevant official, updated recommendations or guidelines issued by the competent public health authorities, in order to manage each patient's case in light of the scientifically accepted data pursuant to their respective ethical and professional obligations. It is also the health professional's responsibility to verify the applicable rules and regulations relating to drugs and medical devices at the time of prescription.

© The European Society of Cardiology 2014. All rights reserved. For permissions please email: journals.permissions@oup.com.

^{*} First and corresponding authors: Stephan Windecker, Cardiology, Bern University Hospital, Freiburgstrasse 4, CH-3010 Bern, Switzerland. Tel: +41316324770; Fax: +41316324299; Email: stephan.windecker@insel.ch

Philippe Kolh, Cardiovascular Surgery Department, University Hospital (CHU, ULg) of Liege, Sart Tilman B 35, 4000 Liege, Belgium. Tel: +32 4 366 7163; Fax: +32 4 366 7164; Email: philippe.kolh@chu.ulg.ac.be

 $^{^{\}scriptsize \ddagger}$ Other ESC entities having participated in the development of this document:

ESC/EACTS Guidelines Page 49 of 100

16.3.6 On-pump and off-pump procedures

Despite improved techniques and experience, part of the morbidity related to CABG is caused by the extracorporeal circulation (cardiopulmonary bypass) and access for cardiopulmonary bypass, prompting the off-pump approach. Two recent large, international, randomized trials have shown no difference in 30-day or 1-year clinical outcomes between on- and off-pump surgery, when performed by experienced surgeons. 441,621,622 There is also enough evidence to conclude that, for most patients and surgeons, on-pump CABG provides the best—or equal—short- and long-term outcomes. 621-625 For some surgeons, off-pump CABG is associated with inferior early and late graft patency rates and possibly compromised longterm survival; however, complete off-pump procedures in the hands of highly trained teams appear to be associated with a reduced risk of early morbidity, such as stroke, wound and respiratory infections, as well as fewer transfusions and shorter hospital stay. 626-629 In the subgroup of patients with end-stage CKD, there is some evidence that off-pump CABG is associated with lower in-hospital mortality and need for new renal replacement therapy.³⁸⁰

In the subgroup of patients with atherosclerotic changes of the ascending aorta, a no-touch technique—avoiding any manipulations of the ascending aorta either on- or off-pump—is essential to reduce the risk of stroke. The consistent cross-over rate of around 5% from on-pump CABG to off-pump CABG in high-quality RCTs suggests the necessity of routine ECG-gated CT scans of the thoracic aorta before bypass surgery in patients over 70 years of age or those with other risk factors for extensive atherosclerosis.

16.3.7 Minimally invasive procedures

Minimally invasive direct coronary artery bypass may represent an attractive alternative to a sternotomy. 630 It has a similar safety and efficacy profile to conventional on- and off-pump CABG, with markedly reduced post-operative length of stay and an early quality-of-life benefit, although spreading of the ribs is associated with increased post-operative pain. $^{631-633}$

16.4 Reporting perioperative outcome

Perioperative reporting of outcome after CABG procedures should be done on a risk-adjusted basis. Early clinical outcome at 3 months after CABG is characterized by a 1-2% mortality rate and a 1-2% morbidity rate for each of the following events: stroke, renal, pulmonary and cardiac failure, bleeding, and wound infections. The early risk period after CABG extends up to 3 months, is multifactorial, and depends on the interface between technical variability and patient comorbidity. 634

17. Procedural aspects of percutaneous coronary intervention

17.1 Percutaneous coronary intervention devices

17.1.1 Balloon angioplasty

Plain balloon angioplasty has been displaced in the treatment of de novo coronary lesions after demonstration of the superiority of

BMS and, more recently, DES in terms of repeat revascularization. 645 Its contribution to the treatment of in-stent restenosis has also diminished after recent studies demonstrated the advantages of DES and drug-coated balloons for this indication. 505,511 However, balloon angioplasty might be a valuable PCI option in all patients in whom implantation of stents is technically not achievable, or in a vessel that is too small to be stented (<2.0 mm), and in patients with critical stenoses who require urgent surgery.

17.1.2 Coronary stents

Bare-metal stents

Coronary stents are very effective in repairing dissections and have eliminated the need for urgent CABG due to abrupt vessel closure. Fully covered stents can be life-saving in the rare event of coronary perforation. The contribution of BMS is its approximately 30% lower rate of restenosis than with plain balloon angioplasty. 645 Although many efforts have been made to further reduce restenosis by modification of stent design and materials, thinning of stent struts has been the only proven modification capable of reducing restenosis of BMS. 646,647 Bare-metal stents have been associated with favourable outcomes in terms of mortality, myocardial infarction, and stent thrombosis. 124 However, owing to a 20-30% rate of recurrence of angiographic stenosis within 6-9 months after implantation, restenosis with BMS has often been referred to as the 'Achilles' heel' of PCI.⁶⁴⁵ There is no indication for BMS over new-generation DES, irrespective of patient and lesion subset. Similarly, there is no clear evidence of a difference between DES and BMS in the risk of stent thrombosis following unplanned disruption of DAPT.⁶⁴⁸

Early-generation drug-eluting stents

The risk of restenosis with BMS led to the development of DES, which consist of a metallic stent platform with controlled release of antiproliferative drugs, mostly controlled by surface polymers. Early-generation DES released sirolimus (e.g. Cypher[®])⁶⁴⁹ or paclitaxel (e.g. Taxus®). 650 Both in native vessels and saphenous vein bypass grafts, DES potently reduced angiographic and ischaemiadriven TVR. 124,495 Thus, the risk of clinical restenosis with the use of early-generation DES was 50-70% lower than with BMS, corresponding to a number-needed-to-treat of approximately 7-8. ¹²⁴ In RCTs, no significant differences were observed in the long-term rates of death or myocardial infarction after use of DES or BMS. 124,199 Despite the superior anti-restenotic efficacy of earlygeneration DES over BMS, concerns have been generated by studies showing an increased propensity for very late stent thrombosis. 244,651,652 Although early-generation DES represented an important advance in the field of PCI,653 they currently play an irrelevant role in the treatment of CAD and are largely supplanted by new-generation DES.³

New-generation drug-eluting stents

New-generation DES are characterized by thin-strut, metallic platforms that release limus-based antiproliferative drugs from durable polymers with improved biocompatibility and lower polymer mass, 654,655 biodegradable polymers, 654,656-658 or polymer-free surfaces. 659,660 Recent studies have shown the superiority of several new-generation DES over early-generation DES, not only with respect to efficacy but also safety. 128,129,661,662 New-generation DES have addressed previous concerns of very late

Page 50 of 100 ESC/EACTS Guidelines

stent thrombosis and are at least as safe as bare-metal stents during long-term follow-up. *Table 10* displays a list of Conformité Européenne (CE)-approved new-generation DES, supported by RCT evidence with clinical endpoints. *Table 11* shows a list of CE-approved new-generation DES, the proven efficacy of which was based on angiographic findings from studies with or without a control group. These tables only provide a temporary 'snapshot' of available products, as new devices will be introduced or new evidence of established devices will become available.

Indications for new-generation DES

Increased efficacy and safety of new-generation DES have enabled their unrestricted use in patients with CAD and an indication for PCI, including patients with diabetes, multivessel and LM disease, acute myocardial infarction, SVG and restenotic lesions, and chronic total occlusions.³ New-generation DES should therefore be considered by default in all clinical conditions and lesion subsets. Among patients who require anticoagulation with NOACs, undergo non-cardiac surgery, experience bleeding complications, or are non-compliant with medication intake, previous concerns relating to differences in the duration of DAPT and risks associated with DAPT cessation are not substantiated in recent data sets.^{648,663}

17.1.3 Bioresorbable stents

Completely bioresorbable stents, which dissolve after fulfilling their support function in the lesion site of the coronary vessel, have been a perennial aim since the introduction of the metallic stents. The combination of resorbable stent platforms with drug-eluting properties has enhanced the efficacy of these devices. Current stent platforms are based on two technologies: the manufacturing of drug-eluting, bioresorbable, polymer-based stents and drug-eluting, resorbable, metallic (magnesium) stents.⁶⁸⁴ The resorption process of the stent platforms takes from several months to 2 years, depending on polymer composition. To date, bioresorbable stents have been shown to dissolve completely over time, to restore the vasomotion of treated segments, and to result in positive remodelling with late lumen enlargement. In small series of patients with relatively simple lesions, early results are promising and appear to be similar to newgeneration DES. 685-687 However, confirmation in large-scale RCTs is required to establish the indications for these devices. Table 12 includes the list of devices approved for use in Europe.

17.1.4 Drug-coated balloons

The rationale of using drug-coated balloons is based on the concept that, with highly lipophilic drugs, even short contact times between the balloon surface and the vessel wall are sufficient for effective drug delivery. Using a paclitaxel-coated balloon, three RCTs, Paclitaxel-Coated Balloon Catheter I (PACCOCATH-I) and PACCOCATH-II, 507,508 and Paclitaxel-Eluting PTCA-Catheter In Coronary Disease (PEPCAD)-II, 689 have targeted in-stent restenosis following BMS implantation, while three others have targeted in-stent restenosis in patients predominantly treated with DES eluting limus-analogues. 509-511 By virtue of the positive results achieved without additional stent implantation, drug-coated balloons may represent an attractive option for patients with restenosis after

implantation of DES, although it is not known whether they are as safe and effective for this indication as new-generation DES that elute limus analogues.

In the randomized PEPCAD III study, the combination of a drugcoated balloon with cobalt chromium stent implantation was inferior to a sirolimus-eluting stent for de novo indications. ⁶⁹⁰ Also, the Drug Eluting Balloon in Acute Myocardial Infarction (DEB-AMI) trial showed that drug-coated balloons followed by BMS implantation were inferior to paclitaxel-eluting stents in patients with STEMI.⁶⁹¹ A recent angiographic study suggested that drug-coated balloons may serve as an alternative to paclitaxel-eluting stents for the treatment of lesions in small coronary vessels;⁶⁹² however, the role of drug-coated balloons in this setting has not been evaluated against more effective, new-generation DES with limus analogues. There are various types of drug-coated balloons approved for use in Europe and their main characteristics are listed in Table 13. Most of the differences are related to the drug carrier, whereas paclitaxel is currently the sole active drug used. Although specifically designed comparative studies are lacking, one cannot assume a class effect for all drug-coated balloons.⁶⁹³

17.1.5 Other devices

Although routine use of rotational atherectomy did not improve outcomes after DES, ⁶⁹⁸ such a device might technically be required in cases of tight and calcified lesions, to allow subsequent passage of balloons and stents. There is a resurgence in the use of rotational atherectomy for the purpose of optimal lesion preparation among patients undergoing implantation of bioresorbable stents.

17.2 Adjunctive invasive diagnostic tools

17.2.1 Intravascular ultrasound

Coronary angiography is unable to visualize the atherosclerotic involvement of the arterial wall. Intravascular ultrasound imaging allows a real-time, tomographic assessment of lumen area and plaque composition, size, and distribution. As a result of diffuse disease and remodelling, coronary angiography underestimates the extent and severity of the disease compared with IVUS. 699 Although invasive by nature, IVUS is the established standard for accurate measurement of plaque burden, and the technique has been systematically used to determine the influence of different drugs on coronary plaque progression or regression. 700,701

Several RCTs addressed the potential of IVUS in reducing restenosis and adverse events after BMS implantation—with conflicting results. Most of these RCTs focussed on optimizing stent expansion using IVUS. Findings from meta-analyses subsequently suggested that better clinical and angiographic results may be obtained under IVUS guidance. To 102–704 In the DES era, a threshold of stent expansion (5.0–5.5 mm²) was proposed to predict the occurrence of late events. In the subset of patients with LM disease, observational studies suggest that IVUS-guided stent implantation is associated with improved survival during long-term clinical follow-up. The use of intracoronary imaging has also been advocated in patients with stent failure, including restenosis and stent thrombosis, in order to explicate and correct underlying mechanical factors. In a multicentre all-comers study to establish the frequency, predictors, and timing

ESC/EACTS Guidelines Page 51 of 100

Table 10 CE-approved new-generation DES recommended for clinical use based on randomized trials with a primary clinical endpoint (in alphabetical order)

DES	Stent platform	Polymer coating	Drug	References		
Based on durable polymer coatings						
Promus element	Platinum-chrome	PBMA and PVDF-HFP	Everolimus	664,665		
Resolute	Cobalt-chrome	PBMA, PHMA, PVP, and PVA	Zotarolimus	655,665,666		
Xience	Cobalt-chrome	PBMA and PVDF-HFP	Everolimus	247, 654,667		
Based on biodegradable polymer coatings						
Biomatrix	Stainless steel	PDLLA	Biolimus A9	248, 668		
Nobori	Stainless steel	PDLLA	Biolimus A9	656,658,669		
Yukon Choice PC	Stainless steel	PDLLA	Sirolimus	<mark>657</mark>		
Orsiro	Cobalt-chrome	PLLA	Sirolimus	961		
Ultimaster	Cobalt-chrome	PDLLA and PCL	Sirolimus	960		

CE = Conformit'e Europ'enne; DES = drug-eluting stent; PBMA = poly n-butyl methacrylate; PDLLA = poly(d,l)-lactic acid; PHMA = polyhexyl methacrylate; PLLA = poly-L-lactic acid; PVA = polyvinyl acetate; PVDF-HFP = poly(vinylidene fluoride-cohexafluoropropylene).

Table II CE-approved DES with angiographic efficacy data from randomized or non-randomized studies (in alphabetical order)

DES	Stent platform	Polymer coating	Drug	References		
Based on durable polymer coatings						
DESyne Nx	Cobalt-chrome	PBMA Novolimus		670		
STENTYS	Nitinol	PSU and PVP	Paclitaxel	671		
Based on biodegradable po	olymer coatings					
Axxess	Nitinol	PDLLA	Biolimus A9	672,673		
BioMime	Cobalt-chrome	PLLA and PLGA	Sirolimus	674		
Combo	Stainless steel	PDLLA and PLGA + Additional coating with anti- CD34	Sirolimus	675		
DESyne BD	Cobalt-chrome	PLLA	Novolimus			
Infinnium	Stainless steel	PLLA, PLGA, PCL, and PVP	Paclitaxel	676		
MiStent	Cobalt-chrome	PLGA	Crystalline sirolimus	677		
Supralimus Core	Cobalt-chrome	PLLA, PLGA, PCL, and PVP	Sirolimus	678,679		
Synergy	Platinum-chrome	PLGA	Everolimus	680		
Polymer-free						
Amazonia Pax	Cobalt-chrome	-	Paclitaxel			
BioFreedom	Stainless steel	-	Biolimus A9			
Cre8	Cobalt-chrome	-	Sirolimus	681		
Yukon Choice PF	Stainless steel	_	Sirolimus	682,683		

 $CE = Conformit\'e Europ\'enne; DES = drug-eluting stent; PBMA = poly n-butyl methacrylate; PCL = poly(L-lactide co-ϵ-caprolactone); PDLLA = poly(d,l)-lactic acid; PLGA = poly(lactide-co-glycolide); PLLA = poly-L-lactic acid; PSU = polysulfone; PVP = polyvinylpyrrolidone.$

Page 52 of 100 ESC/EACTS Guidelines

Table 12 Bioresorbable stents providing drug-elution with angiographic efficacy data from non-randomized studies (in alphabetical order)

Device	Delivery platform	Polymer	Drug	References
Absorb BVS	PLLA	PDLLA	Everolimus	685,686
DESolve	PLLA	PLLA	Novolimus	688
DREAMS	Magnesium alloy	PLGA	Paclitaxel (revised version Sirolimus)	687

PDLLA = poly(d,l)-lactic acid; PLGA = poly(lactide-co-glycolide); PLLA = poly-L-lactic acid.

Table 13 CE-approved drug-coated balloons (in alphabetical order)

Device	Carrier	Drug	References
Danubio	ВТНС	Paclitaxel	-
Dior II	Shellac	Paclitaxel	694,695
Elutax	-	Paclitaxel	693
IN.PACT Falcon	Urea	Paclitaxel	692
Моху	Polysorbate	Paclitaxel	696
Pantera Lux	BTHC	Paclitaxel	697
Protégé NC	BTHC	Paclitaxel	-
SeQuent Please	lopromide	Paclitaxel	507–511

 ${\it BTHC = butyryl-tri-hexyl\ citrate;\ CE = Conformit\'e\ Europ\'eenne.}$

of stent thrombosis, a pre-specified substudy compared outcomes of IVUS against angiographic guidance of DES implantation. IVUS-guided DES implantation (pre- and post-PCI in 63% of included cases) was performed in 3349 of 8583 patients (39%). In propensity-adjusted multivariable analysis, IVUS guidance was associated with reduced rates of definite or probable stent thrombosis (adjusted HR 0.40; 95% CI 0.21–0.73; P=0.003), myocardial infarction (adjusted HR 0.66; 95% CI 0.49–0.88; P=0.004), and MACE (adjusted HR 0.70; 95% CI 0.55–0.88; P=0.003) at 1 year. Notable limitations of this study were the lack of randomization and lack of pre-specified guidelines for performing and acting on IVUS findings.

In addition to conventional grey-scale IVUS, other ultrasound-based techniques have been used to provide additional diagnostic insights. Assessment of plaque composition may be further improved by analysis of the complete radiofrequency signal using different diagnostic algorithms, including those used in 'virtual histology'.

17.2.2 Optical coherence tomography

Optical coherence tomography is a light-based modality of intravascular imaging with higher spatial resolution than IVUS (15 vs. 150 μ m) and is ideally suited to accurate detection of intraluminal structures. Plaque composition, including the presence of lipid pools and

intraluminal thrombi, can also be determined. 707 Notably, this is the only technique capable of providing accurate measurements of the thickness of the fibrous cap and to detect even minor cap disruptions. 707,708 Early stages of cardiac allograft vasculopathy are frequently angiographically silent, yet can be visualized with OCT or IVUS and are associated with important prognostic implications. 708 Optical coherence tomography requires complete blood clearance from the lumen for imaging, has a limited penetration on the vessel wall and is therefore unable to assess the complete plaque burden. After stent implantation, OCT is more accurate than IVUS in detecting subtle morphological details including malapposition, residual thrombus, plaque prolapse, and residual dissections, although the clinical significance of these findings remains to be determined. 709,710 During longitudinal follow-up investigations, OCT is more accurate than IVUS for assessing even neointimal thickness, strut apposition, and coverage. These findings are important surrogate markers of the efficacy and safety of DES and are frequently used to compare new DES. A recent retrospective and observational study suggested that OCT-guided stenting might improve clinical outcomes.⁷¹¹ Owing to its very high resolution, OCT is used to reveal the underlying mechanisms in patients with stent failure, including in-stent restenosis and stent thrombosis. 516 Likewise, intrastent neointimal tissue may be characterized, including the detection of